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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/544,145	12/22/2006	Shyam S. Mohapatra	USF.T192XC1	1541

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EXAMINER
LONG, SCOTT

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
02/01/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/544,145	MOHAPATRA, SHYAM S.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,8,10,12,16-21,24-34,37-40 and 42-48* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,12,16,24,30-32,39,43 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,3-5,7,8,17-21,25-29,33,34,37,38,40,42,44-46 and 48.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks and Claim amendments, filed on 28 September 2009. The examiner also acknowledges the response to restriction filed on 29 January 2010.

Claim Status

Claims 1, 3-5, 7, 8, 10, 12, 16-21, 24-34, 37-40 and 42-48 are pending. Claims 2, 6, 9, 11, 13-15, 22-23 and 41 are cancelled. Claims 1, 5, 10, 16, 17, 20 and 37-40 are amended. Claims 42-48 are newly added. Claims 1, 3-5, 7, 8, 17-21, 25-29, 33, 34, 37, 38, 40, 42, 44-46 and 48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/19/2010. Claims 10, 12, 16, 24, 30-32, 39, 43 and 47 are under current examination.

Priority

This application claims benefit as a 371 of PCT/US04/04262 (filed 02/13/2004) which claims benefit of 60/319,946 (filed 02/14/2003) and claims benefit of 60/319,956 (filed 02/19/2003). The instant application has been granted the benefit date, 02/14/2003, from the application 60/319,946.

Election/Restrictions

Applicant's election with traverse of group II (claims 10, 12, 16, 24, 30-32, 39, 43 and 47) in the reply filed on 29 January 2010 is acknowledged.

The applicant has argued that the art cited by the examiner in the Lack of Unity does not "anticipate" in the instant invention. As the examiner applied the cited art under the PCT treaty Lack of Unity Rules and not under 35 USC 102, the examiner finds the applicant's argument unpersuasive. Furthermore, the examiner has found *a posteriori* that compositions comprising condensed DNA/lipopolyplexes is not a technical feature that defines a contribution of the prior art.

Therefore, the requirement is deemed proper and is therefore made FINAL.

RESPONSE TO ARGUMENTS

35 USC § 112-2nd

The rejection of claim 39 under 35 USC 112, 2nd paragraph is withdrawn in response to the applicant's claim amendments. The applicant's claim amendments have been fully considered and are persuasive. Therefore, the examiner hereby withdraws the rejection of claim 39 under 35 USC 112, 2nd paragraph.

35 USC § 103

Hart & Ni

The rejection of claims 10, 12, 16, 24, 30-32, and 39 under 35 U.S.C. 103(a) as being unpatentable over Hart (Exp. Opin. Ther. Patents. 2000; 10(2): 199-208) in view of Ni et al (US2002/0151009, published 17 October 2002) is withdrawn in response to the applicants arguments and/or claim amendments. The applicant's arguments and claim amendments have been fully considered and are persuasive. Therefore, the examiner hereby withdraws the rejection of claims 10, 12, 16, 24, 30-32, and 39 under 35 U.S.C. 103(a) as being unpatentable over Hart in view of Ni et al.

Yu & Vijayanathan

The rejection of claims 10 and 39 under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (US2003/0186916, published 2 Oct 2003) in view of Vijayanathan et al. (*Biochemistry*. Dec.3, 2002, 41(48):14085-14094) is withdrawn in response to the applicants arguments and/or claim amendments. The applicant's arguments and claim amendments have been fully considered and are persuasive. Therefore, the examiner hereby withdraws the rejection of claims 10 and 39 under 35 U.S.C. 103(a) as being unpatentable over Yu et al. in view of Vijayanathan et al.

Hart, Ni & Vijayanathan

The rejection of claims 29 and 37-41 under 35 U.S.C. 103(a) as being unpatentable over Hart (Exp. Opin. Ther. Patents. 2000; 10(2): 199-208) in view of Ni et al (US2002/0151009, published 17 October 2002) as applied to claims 1, 5, 10, 17, and 21 above, and further in view of Vijayanathan et al. (*Biochemistry*. Dec.3, 2002, 41(48):14085-14094) is withdrawn in response to the applicants arguments and/or claim amendments. The applicant's arguments and claim amendments have been fully considered and are persuasive. Therefore, the examiner hereby withdraws the rejection of claims 10, 12, 16, 24, 30-32, and 39 under 35 U.S.C. 103(a) as being unpatentable over Hart in view of Ni et al. and further in view of Vijayanathan et al.

NEW GROUNDS OF REJECTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 10, 12, 16, 24, 30-32 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boussif et al. (EP1013772, published 28 June 2000).

Claim 10 is directed to a method for delivery and expression of a polynucleotide to respiratory epithelium of a mammal, said method comprising administering a nanoparticle to the respiratory epithelium, wherein the nanoparticle comprises a complex of chitosan, or a chitosan derivative, a lipid, and a polynucleotide, wherein said polynucleotide is expressed in the respiratory epithelium, wherein said nanoparticle induces production of less interleukin-6 compared to a particle comprising a complex of the chitosan, or chitosan derivative and the polynucleotide without the lipid.

Boussif et al. teach methods of gene therapy (page 15, parag.0081, lines 41-42) to respiratory epithelium (page 15, parag.0079, line 37) using nanoparticles (page 8, parag.0042) comprising lipopolyplexes (page 7, lines 37-38). Boussif et al. teach that the cationic polymer can be chitosan (page 9, parag.0051, line 45). Accordingly,

Boussif et al. suggest the gene therapy method comprising delivery to respiratory epithelium by administering the lipopolyplex (i.e., DNA+chitosan+lipid) nanoparticle described in claim 10.

In previous remarks, the applicant has argued that the following limitations must be taught by the cited art: "wherein said nanoparticle induces production of less interleukin-6 compared to a particle comprising a complex of the chitosan, or chitosan derivative and the polynucleotide without the lipid." The examiner notes that Figure 4 of the specification show the amount of IL-6 induced by polyplexes (DNA+chitosan), lipoplexes (DNA+lipid), and lipopolyplexes (DNA+chitosan+lipid). The graph of Figure 4 shows that polyplexes induce the most IL-6, lipoplexes induce the least IL-6 and lipopolyplexes induce an amount of IL-6 between the other two formulations. Therefore, the examiner concludes that as the lipopolyplexes comprise a blend of both chitosan and lipid, it is not surprising to find that the amount of IL-6 induced falls between the other two formulations. Accordingly, it is entirely predictable that a lipopolyplex induces less IL-6 than a polyplex and more IL-6 than a lipoplex.

Claim 12 is directed to the method of claim 10, wherein the polynucleotide encodes a cytokine. Boussif et al. teach administering a polynucleotide encoding various cytokines, including interferon (page 12, parag.0063, line 12).

Claim 16 is directed to the method of claim 10, wherein the nanoparticle is administered within a composition comprising a pharmaceutically acceptable carrier. Boussif et al. teach pharmaceutical compositions of the invention (page 14, parag. 71, line 33).

Claim 24 is directed to the method of claim 10, wherein the particle is administered intranasally. Boussif et al. describe intranasal administration of DNA complexes and thereby suggest such a method (page 3, parag.0030, line 33).

Claim 30 is directed to the method of claim 10, wherein said particle comprises a chitosan derivative. Boussif et al. suggest chitin derivatives (page 9, parag.0050, line 47). Furthermore, using a derivative of a component of a composition would be an obvious variant.

Claim 31 is directed to the method of claim 10 wherein the mammal is human. Boussif et al. teach treating the human body (page 14, parag.0073, line 39).

Claim 32 is directed to the method of claim 10, wherein said particle is administered to the respiratory tract of the mammal. Boussif et al. teach treating lung.

Claim 43 is directed to the method of claim 10, wherein said lipid is a cationic lipid. Boussif suggest nanoparticles comprising lipopolyplexes, wherein the lipids are cationic lipids.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to use a lipopolyplex composition of chitosan, a lipid, and a polynucleotide for delivery (and expression) of a polynucleotide to the respiratory epithelium of a mammal.

The person of ordinary skill in the art would have been motivated to use this method because Boussif et al. suggest lung gene therapy encompassing such nanoparticle lipopolyplexes. Boussif has indicated that these nanoparticles are stable and have high transfection efficiency.

An artisan would have expected success, because formulating polylipoplexes were known in the art prior to the instant application and Boussif suggests that the lipopolyplexes would be advantageous for delivering nucleic acids to respiratory epithelium.

Therefore the methods as taught by Boussif et al. would have been *prima facie* obvious over the methods of the instant application.

Boussif & Vijayanathan

Claim 39 rejected under 35 U.S.C. 103(a) as being unpatentable over Boussif et al. (EP1013772, published 28 June 2000) as applied to claim 10 above, and further in view of Vijayanathan et al. (*Biochemistry*. Dec.3, 2002, 41(48):14085-14094)..

The teachings of Boussif are recited above in the previous 35 USC 103 rejection.

Boussif fails to teach the limitations of claim 39, directed to "wherein said polynucleotide is surrounded by a monolayer of lipid, and wherein said nanopoarticle comprises a plurality of polynucleotide-lipid inverted cylindrical micelles arranged in a hexagonal lattice.

Vijayanathan et al. teach that non-viral delivery vehicles comprising polycationic lipids and cationic polymers (including chitosan) condense DNA into nanoparticles having columnar hexagonal liquid crystalline structures. Further, Vijayanathan teach that the particles mimic the cytoplasmic monolayer of the plasma membrane. Since the teachings of Vijayanathan et al. encompass nanoparticles comprising the same

materials as Boussif et al. and the instant claims, the examiner concludes the arrangement of such nanoparticles into a hexagonal lattice is a natural consequence of the chemical nature of these particles.

No rationale for obviousness is required since Vijayanathan demonstrates the limitations of claim 39 are an intrinsic characteristic of the nanoparticles described. The limitations of claim 39 do not provide additionally active steps which further limit the claimed method. Accordingly, the limitations of claim 39 are obvious.

Furthermore, MPEP 2112 indicates "something which is old does not become patentable upon the discovery of a new property." It is the applicant's duty to show unobviousness of the limitation of claim 39.

Therefore the methods as taught by Boussif et al. and Vijayanathan et al. would have been *prima facie* obvious over the methods of the instant application.

Boussif & Han

Claim 47 rejected under 35 U.S.C. 103(a) as being unpatentable over Boussif et al. (EP1013772, published 28 June 2000) as applied to claim 10 above, and further in view of Han et al. (Molecular Therapy. October 2000; 2(4): 302-317).

The teachings of Boussif are recited above in a previous 35 USC 103 rejection.

Boussif fails to teach the limitations of claim 47, directed to "wherein said administering of said nanopoarticle achieves higher transfection efficiency compared to administration of each of : (a) polynucleotide alone, (b) a complex of said polynucleotide

and said chitosan or chitosan derivative, and (c) a complex of said polynucleotide and said lipid."

Han et al. teach "as has been noted, the transfection efficiency of aggregated large size complexes [DNA + lipid] is low. To reduce the particle size of the complex, cationic polymers such as PLL was used to precondense DNA and then mixed with cationic liposomes for complex formation, leading to the formation of small size (<100 nm) complexes and enhanced transfection efficiency" (page 308, col.1, Lipopolyplex-based Systems, and Fig.3, emphasis added by examiner). Throughout, Han et al. it is indicated that naked DNA has the lowest transfection efficiency compared to formulated DNA. Formulations of DNA and chitosan were found to be higher transfection efficiently than DNA/PEI and lower transfection efficiently than DNA/PLL (page 305). Taken as a whole, the teachings of Han et al. demonstrate that polylipoplex nanoparticles are highly efficient transfection agents and suggest that they may be superior to the formulations compared in instant claim 47.

The limitations of claim 47 require testing of the nanoparticle used in the instant method. The limitations of 47 do not recite a further active method step of claim 47. Rather they suggest an intrinsic (and relative) characteristic of the nanoparticle. As such, they do no provide guidance to a skilled artisan on how to practice the method of gene delivery and expression. Rather, the limitations of claim 47 seem directed to a method of characterizing the lipopolyplexes. A skilled artisan would understand the characteristics of the nanoparticles used in a method of treatment, because this is typically performed during preclinical studies of an investigational new drug.

No rationale for obviousness is required since Han demonstrates the limitations of claim 47 are an intrinsic characteristic of the nanoparticles described. The limitations of claim 47 do not provide additional active steps which further limit the claimed method. Accordingly, the limitations of claim 47 are obvious.

Furthermore, MPEP 2112 indicates "something which is old does not become patentable upon the discovery of a new property." It is the applicant's duty to show unobviousness of the limitation of claim 47.

Therefore the methods as taught by Boussif et al. and Han et al. would have been *prima facie* obvious over the methods of the instant application.

Conclusion

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Scott Long/
Patent Examiner, Art Unit 1633